

no significant difference between the performances of heat-stable and control vaccines of similar viable count.

Discussion

We have shown above that B.C.G. cells grown in a medium in which no glycerol is present survive the process of freeze-drying to a much greater extent, and when so dried have a much greater resistance at elevated temperatures than those grown on media containing glycerol. This finding is in accordance with the hypothesis that some metabolic product of glycerol, at present unidentified but probably an aldehyde or pyruvate, has a toxic action on the B.C.G. cells in the dried state. Glycerol itself would not appear to be incriminated, since the addition of glycerol to the freeze-drying menstuum for cells grown in the absence of glycerol had no adverse effect. It seems possible that the metabolic product of the glycerol contains a carbonyl group capable of reacting to form a toxic "browning reaction" compound in the manner described by Scott (1960).

Laboratory tests and tests on experimental animals have shown that, apart from surviving better during the freeze-drying process and on storage in the dried state, the B.C.G. cells grown in the new glycerol-free medium have the same biological properties as those grown on Sauton's medium containing glycerol. After this finding it seemed justified to compare on babies the relative tuberculin-sensitizing powers of the heat-stable and control vaccines; the results have shown that the effects of the two types of vaccine are identical. Further, the two types of vaccine give the same incidence of local reactions at the vaccination site. We therefore conclude that the heat-stable vaccine would be as acceptable for vaccination as the more thermolabile vaccine it is meant to replace.

The increased resistance to heat of the new vaccine will have obvious advantages in the field. Normal unrefrigerated transportation will generally be permissible, and accidental short exposure to even relatively high temperatures should not prove disastrous to the efficacy of the vaccine. It is not suggested that the vaccine is so stable as to permit abuse of recommended storage conditions; it should, however, enable fully viable B.C.G. vaccine to reach persons living in remote districts in tropical and subtropical countries, where they might otherwise be denied the protection afforded by B.C.G. vaccination.

Summary

A method is described for preparing freeze-dried B.C.G. vaccine with increased stability to heat.

The method involves growing the B.C.G. cells from which the vaccine is prepared in a glycerol-free medium. The hypothesis is advanced that absence of some toxic product of glycerol metabolism permits this stability.

Apart from a greater stability to heat, the new vaccine has the same biological properties as a control vaccine of the same viability prepared in conventional culture media.

Batches of heat-stable and control vaccines of the same viability have the same allergenic properties when used to vaccinate babies and produce similar local reactions at the vaccination site.

The more heat-stable vaccine will have obvious advantages for distribution and use in tropical and subtropical countries.

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ELECTROENCEPHALOGRAPHIC STUDIES IN TRIPLE-IMMUNIZED INFANTS

BY

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The problem of cerebral complications following triple or pertussis immunization has been very much debated in Sweden since 1959, when Ström at a meeting presented an alarming series of cases, where symptoms of severe brain injury had followed the immunization procedure. The report appeared in this journal (Ström, 1960). In a letter to the Editor shortly afterwards (Malmgren *et al.*, 1960) it was claimed that Ström had shown an uncritical attitude when accepting a connexion between the immunization and the symptoms indicating brain damage in several cases. These objections were partly based on a report of a committee appointed by the Royal Medical Board, in which the incidence of permanent damage to the central nervous system was calculated to be 1 in 50,000 as compared with Ström's figure of 1 in 16,000. A short review of the problem including a preliminary report on some electroencephalographic studies has been published in Swedish (Hellström, 1962). The present paper deals with a more detailed account of these observations.

In a previous investigation by Low (1955) comprising 83 infants, where the E.E.G. was recorded after pertussis or triple immunization, one case was found with a marked slowing in all leads during some days afterwards. In one week the E.E.G. again became normal. In another case less marked and more questionable changes were noted. It was concluded that mild but possibly significant cerebral reactions may occur in connexion with pertussis immunization.

Electroencephalography has also been used as a tool to detect subclinical cerebral reactions in connexion with

other immunization procedures. In recent investigations this has been done after smallpox vaccination with a positive finding in a number of cases (Radtke, 1961), in polio vaccination with negative results (Gibbs and Gibbs, 1958), and after immunization with live attenuated measles virus vaccine (Gibbs *et al.*, 1961). In the last-mentioned study one of 22 children showed an increase in slow-wave activity in the occipital region, but the transient changes were attributed to an intercurrent respiratory-tract infection rather than to the measles vaccination.

Material and Methods

In 84 healthy infants, 3 to 12 months of age, staying in an infants' home, whose parents requested a triple immunization, E.E.G. examinations were done within three days before and six and 24 hours after, and in 60 cases also one week after the vaccination. In 82 cases the study was done in connexion with the first injection, in two with the second. The temperature was measured immediately before the E.E.G. examination. Eight additional patients, aged 4 to 8 months, had been referred to our paediatric department because of unusual general reactions appearing after the first injection in six cases and after the second in two. The reactions consisted of high fever lasting more than two days in seven infants and pallor and a transient shocklike state in one, this reaction occurring a few hours after the injection and lasting for about an hour. In four of the seven infants with high fever the temperature dropped on the third or fourth day and a macular rash appeared. A total and differential white-blood-cell count showed leucopenia and a relative lymphocytosis, making the diagnosis of a coincidental roseola infantum highly probable. In a fifth febrile infant a urinary-tract infection was present. In these eight infants an E.E.G. was done one to four days after the immunization, being repeated during subsequent days in some of them.

Subcutaneous injections of 1 ml. of commercial triple-vaccine were given. The vaccine was delivered by the State Bacteriological Laboratory and contained merthiolate-killed pertussis bacilli, diphtheria and tetanus toxoid adsorbed to aluminium phosphate, and a local anaesthetic.

All the records were made with the aid of an Offner-Type T electroencephalograph with eight channels. A bipolar record, using 16 silver-plate electrodes attached with collodion according to a modified 10/20 system (Hellström *et al.*, 1962) was used. Light sedation was sometimes accomplished with 5–10 mg. of promethazine chloride. The recording lasted for at least one-half to one hour and in most of the infants during both sleep and wakefulness.

In evaluating the records parts of the different examinations were compared when the infant was awake and when asleep, with sleep spindles well developed in the record. When doing this the investigator was not aware of the examination from which the record had been derived. Special attention was paid to the occurrence of slow-wave activity and to differences in the frequencies of the background activity.

Results

Among the 84 infants examined both before and after the injections a slight-to-moderate febrile reaction was common, with the temperature reaching or exceeding 38° C. (100.4° F.) six hours after vaccination in 33 cases and persisting after 24 hours in 14 cases, but dropping to

normal levels within a further one to two days. No convulsions or other alarming reactions occurred.

In the majority of cases there was a close agreement among the E.E.G.s from the different examinations regarding the general pattern, frequencies of background activity, amplitudes, elements of scattered slow waves, appearance of sleep spindles, etc. Most infants showed fairly uniform patterns throughout the waking or sleeping records respectively; in others, however, considerable variations, especially in the incidence of slow-wave activity, could occur within the same record, apparently due to variations in alertness or depth of sleep. This sometimes made comparison between the results from the different examinations rather intricate. No case was encountered, however, where there was a marked change in the general pattern, in the incidence of slow waves or asymmetry, or where pathological changes were observed in any record as compared with those from the other examinations. Variations in this respect could occur to a certain degree from one examination to another, but as these questionable abnormalities were sometimes seen in the records made before the vaccination these variations could not be interpreted as evidence of a postvaccinal cerebral reaction. In one case a cortical sharp-wave focus was found in the records, both prior to and after the vaccination, apparently representing a subclinical epileptogenic focus.

The records from the eight cases showing the general reactions, and examined only after the immunization, did not reveal any pathological pattern when compared with the control material of healthy infants of corresponding ages before the vaccination.

Discussion

It may be concluded from this study that subclinical cerebral reactions following triple immunization in healthy infants with the vaccine used must be rare. Nor does the investigation by Low (1955) indicate that these could be expected to any greater extent. The experiences from the present study underline the difficulties in comparing records from different examinations of the same patient in this age-group, as considerable variations occur, especially concerning the incidence of slow-wave activity. This variability, probably caused by different levels of alertness and sleep and other factors difficult to control, necessitates great caution in labelling a change in this respect as pathological.

Most of the observations in the present study were made in connexion with the first of three injections, and it is possible that cerebral reactions occur more often after the second and third ones. In the series presented by Ström (1960), however, clinical reactions, including febrile convulsions, were distributed on all three occasions.

There can be no question, however, that the electroencephalogram is a sensitive tool in discovering subclinical acute cerebral disturbances. One of the most convincing examples of this is the report by Gibbs *et al.* (1959), in which the incidence of significant abnormalities in the electroencephalogram during the course of natural measles is stated to be about 50% without clinical evidence of encephalitis. In most cases the abnormal slow-wave activity subsided, but persistent abnormalities were occasionally encountered, and these correlated with clinical evidence of impaired central-nervous-system function.

The present study was made in healthy infants. The possibility remains that infants with previous brain damage would exhibit a greater incidence of E.E.G. changes or an accentuation of previously existing abnormalities. One case of the present series by coincidence had a pre-existing subclinical epileptogenic focus, but the E.E.G. after the immunization did not change. A larger series of pathological cases would, of course, be necessary to allow any conclusions in this respect. For practical purposes this question is of less importance as, at least in Sweden, vaccination in these brain-damaged infants is usually not recommended, although the opposite opinion has also been expressed regarding the greater hazards for these children if they develop pertussis.

The present series is not large when related to the incidence of clinical manifestations. Ström (1960) reported a total incidence of reversible and permanent complications from the central nervous system to be 1 in 6,000; the British Medical Research Council's (1959) figure for convulsions taking place within three days was 1 in 3,500. Electroencephalography is, however, a laborious and time-consuming procedure and has to be used as a complement to the larger field studies and has necessarily to comprise smaller selected groups.

Such a group, which it seems well worth while to explore with E.E.G. examinations, consists of cases having shown more unusual general reactions, such as high prolonged fever, drowsiness, marked irritability, vomiting, and other symptoms indicating a possible central-nervous-system reaction. Eight such cases, seven of them showing prolonged fever, were examined in this material, all without any E.E.G. evidence of brain affection. In five of them an intercurrent infection was demonstrated as a probable cause of the prolonged fever.

The practical value of the negative results reported from the present investigation as an argument for continued pertussis and triple immunization in Sweden is limited. Other approaches are probably more important, such as a critical evaluation of each suspected case of encephalopathy following immunization by a neuropaediatrician. In such cases electroencephalography, to be performed as soon as possible, is of great value. In Sweden such cases have to be reported to the Royal Swedish Medical Board.

Summary

Eighty-four healthy infants were examined by means of electroencephalography before and at certain intervals after triple immunization. An additional eight cases suspected of an acute cerebral reaction following the vaccination were also investigated. None of the infants showed any significant change in the E.E.G. The variability of the E.E.G. pattern in this age-group is stressed.

Neurological complications of pertussis immunization represent rare and unpredictable immunological accidents, and there is no evidence that the brain is in any way affected by the vast majority of such injections.

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SUICIDE IN WESTERN NIGERIA*

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The study of suicide is instructive from many points of view. It is particularly illuminating in this part of the world, since there is no record of any such previous study. Tooth's (1950) study was limited to his Gold Coast Mental Hospital population, and was mainly concerned with the rarity of depressive illness in that country.

Suicide is often committed by people suffering from mental disorder, and for this reason it can be an index of mental ill-health in a community. Schizophrenia and psychoneurosis, with depressive components, and uncomplicated depression are common causes of suicide, and it is these depressive forms of mental illness that have been reported to be rare in Africans. Laubscher (1951), who made an investigation of suicide in South Africa over a two-year period, found only 14 cases in a population of 870,000—less than 1 per 100,000. Carothers (1953) also found few cases of depression in East Africa. Tooth (1950) reported the same experience from the Gold Coast. Benedict and Jacks (1954), in their review of the psychiatric literature on Africa, pointed out that the rarity of depressive illness was reflected in the extremely low suicide rates (under 1 per 100,000, as compared with rates of 10–16 in the United States and rates as high as 25 per 100,000 in Denmark).

On the other hand, Field (1960) pointed out that depression is the commonest mental illness among Akan rural women, and she explained how the erroneous idea of its rarity originated. Lambo (1956, 1960) described the misleading overlay of psychosomatic symptoms in depressive states. In his earlier paper he stated that suicide "is rare, but in association with certain religions and cults is not uncommon"; in his paper of 1960 he was more cautious.

In view of the controversial views on the prevalence of depression, this study, using suicide as a pointer, may throw further light on the subject.

The most recent work on suicide in Africa is that edited by Bohannon (1960), but this is a sociological study covering a wide geographical area. Furthermore, the only study in West Africa reported in the book was concerned with homicide and not suicide.

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